

Attorney Docket No.: RO0006US.NP  
Inventors: Sheu et al.  
Serial No.: 10/580,803  
Filing Date: November 24, 2006  
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#### REMARKS

Claims 1-12, 14-45 and 55-57 are pending in the instant application. While the Office Action Summary indicates that claims 1-12 and 14-45 have been rejected and claims 55-57 have been withdrawn from consideration, the Detailed Action indicates that claims 1-12, 14-45 and 55-57 have been rejected. Claims 1, 14-25, and 30-31 have been amended. Claims 2-11, 33-45 and 55-57 have been canceled. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

#### **I. Rejection of Claims Under 35 U.S.C. §112**

Claims 1-12, 14-45 and 55-57 have been rejected under 35 U.S.C. 112, first paragraph. The Examiner suggests that while the specification is enabled for a method of testing for an anti-oxidant protective effect of a few choline esters of the compounds glutathione, N-acetyl cysteine and cysteine, the specification is not enabled for the very large number of alternative structures, the biological testing thereof and all of the alternative syntheses claimed therefore. Specifically, it is suggested that not all compounds within the scope of the claims have been structurally identified, synthesized and/or tested for the capability to inhibit the adverse effects of oxidants on cell functions. The Examiner acknowledges that the subject matter of claims 1-12, 14-32 and 55-57 are reasonably well enabled; however, it is suggested that no claimed compound has been tested to determine activity in the treatment of any specific disease condition as in claims 33-45 and there is necessarily a high level of skill in determining whether the instant results are

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extrapolatable to the treatment of actual disease conditions of the kind listed in claim 40 or the effective inhibition of "oxidative stress" in the mammalian cells types listed in claims 38 and 45.

Applicants respectfully disagree with this rejection. At the outset, Applicants respectfully wish to point out that contrary to the Examiner's suggestion that Applicants have not demonstrated "treatment of actual disease conditions of the kind listed in claim 40", Example 7 at pages 29 of the specification specifically shows that mitochondrial targeted N-acetyl-L-cysteine improves post-ischemic recovery in rat heart subjected to ischemia-reperfusion, a disease condition specifically listed at line 4 of claim 40. Thus, Applicants have in fact demonstrated treatment of a disease condition of the kind listed in claim 40. However, in the interest of placing the claims in better form for consideration and facilitating the prosecution of this application, Applicants have canceled claims 33-45 without prejudice, reserving the right to file continuing applications for the canceled subject matter. In light of these amendments to the claims, it is respectfully submitted that the subject matter of the claims as currently presented meets the enablement requirement under 35 U.S.C. 112, first paragraph. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

Claims 1-11, 31, and 55-57 have been further rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Specifically, it is suggested that claim 1 recites the term "comprising," which renders the claim indefinite because said term implies that the remainder of the claim fails to completely

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define the subject matter, e.g., that the noted term of art "comprising" implies that the "compound" being defined "includes" undefined structural elements. The Examiner suggests replacement of "comprising" with "having the structural formula" as one way to address the instant rejection. Applicants respectfully disagree. However, in the interest of facilitating the prosecution of this application, the claims have been amended to replace "comprising" with "having." In light of this amendment, it is respectfully requested that this rejection be reconsidered and withdrawn.

Regarding claim 1, it is further suggested that the terms "amino acid" and "amino acid derivative group having antioxidant activity" are incompletely defined because the structural identity or identities of the "derivatives" and the identity or identities of the functional groups responsible for the "antioxidant activity" have not been defined with particularity. Applicants respectfully disagree. However, in the interest of placing the claims in better form for consideration, claims 2-10 have been canceled and claim 1 has been amended to specifically recite exemplary amino acids, amino acid derivatives and peptides for R. Support for this amendment is found in claims 5 and 10 as originally filed, paragraphs [0028]-[0029] and [0036] of the specification, and the known synonyms of glutathionine and L-carnosine as evidenced by the National Institutes of Health PubChem database (enclosed herewith). In light of this amendment, it is respectfully requested that this rejection be reconsidered and withdrawn.

With respect to claim 31, it is suggested that the term "pyrrolyl" is a heteroaromatic ring substituent and cannot

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accommodate variable  $Q^2$ . The Examiner suggests moving the term "pyrrolyl" from claim 31 to claim 30. Applicants have made the appropriate amendment to the claims and therefore respectfully request that this rejection be withdrawn.

In claim 55, it is suggested that the terms "R" and "R'" are not defined as specific chemical structures or even generic chemical structures, nor are the particular protecting group or groups to be removed. Applicants respectfully disagree with this rejection. However, in the interest of facilitating the prosecution of this application, Applicants have canceled claims 55-57 without prejudice, reserving the right to file continuing applications for the canceled subject matter. In light of these amendments to the claims, it is respectfully requested that this rejection be reconsidered and withdrawn.

Claims 14-25 have been rejected under 35 U.S.C. 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claims. Specifically, it is suggested that these claims are dependent from now canceled claim 13 and are therefore improperly dependent. In an earnest effort to clarify, claims 14-25 have been amended to refer to claim 1. In light of this amendment, it is respectfully requested that this rejection under 35 U.S.C. 112, fourth paragraph, be withdrawn.

## **II. Objection to the Claims**

Claims 1, 11, 33, 36, 43 and 55 have been objected to. With respect to claims 1, 33 and 55, it is suggested that the structures labeled as "(I)" and "(II)" are presented as cations

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only, not as compounds. The Examiner suggests that Applicants have failed to include the monovalent anionic counter ions ( $--X^-$ -, plus definition thereof) necessary to meet the minimum definitional requirements of the term "compound" at line 1.

As disclosed in paragraph [0037] and Figure 2, the compounds of the invention have  $Br^-$ ,  $I^-$ , or  $Cl^-$  as monovalent anionic counter ions. Accordingly, in an earnest effort to clarify, Applicants have amended claim 1 to include  $Br^-$ ,  $I^-$ , or  $Cl^-$  as monovalent anionic counter ions to the cations shown therein. In so far as claims 33 and 55 have been canceled, it is respectfully submitted that the objection to these claims is moot.

Regarding claims 11, 36 and 43, it is suggested that the last two listed compounds are not correctly named. Applicants respectfully disagree with this rejection. However, in the interest of facilitating the prosecution of this application, claims 11 have been canceled. In so far as claims 36 and 43 have been canceled, it is respectfully submitted that the objection to these claims is moot.

In light of these amendments, it is respectfully requested that these objections to the claims be reconsidered and withdrawn.

### **III. Double Patenting**

Claims 1-12, 14-45 and 55-57 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 11/312,873. It is acknowledged that the conflicting claims are not identical; however it is suggested that they are not patentably distinct because defined amino acid-choline ester

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derivatives, the pharmaceutical compositions thereof, the method of treatment wherein said amino acid-choline ester derivatives are administered, and the method of making said amino acid-choline esters are directed to substantially overlapping subject matter. The Examiner indicates that this a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants respectfully disagree with this rejection. In particular, it is respectfully submitted that while the instant application provides amino acid-choline ester derivatives, copending Application No. 11/312,873 provides choline ethers and amide analogs of choline esters and N-heterocycle esters as delivery moieties of amino acid-based antioxidant moieties. As such, the '873 disclosure provides compounds distinct from those of the instant invention. Therefore, it is respectfully requested that this rejection be held in abeyance until allowable subject matter has been identified in copending Application No. 11/312,873.

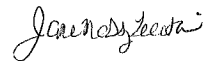
#### **IV. Conclusion**

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

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favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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